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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/351,862	07/12/1999	PHILIP E. THORPE	4001.002282	1339

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PEREGRINE PHARMACEUTICALS, INC.
5353 WEST ALABAMA
SUITE 306
HOUSTON, TX 77056

EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/351,862	THORPE ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,20-30 and 34-49* is/are pending in the application.

4a) Of the above claim(s) *2,13,30,36-38 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,14,20-29,34,35 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6/21/04, 10/8/04, 10/29/04, 11/19/04, 12/8/04, 2/1/05, 7/1/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

RE: Thorpe *et al*

1. The examiner of the application has changed. This case has now been transferred as of 8/17/2005. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Christopher Yaen, Group Art Unit 1643.

2. The amendments filed 12/9/2004 are acknowledged and entered into the record. Accordingly, claims 15-19 and 31-33 are canceled, and claim 49 is newly added.

3. Claims 1-14,20-30, and 34-49 are pending, claims 2,13,30,36-38, and 49 are withdrawn from further consideration as being drawn to a non-elected subject matter.

4. Claims 1,3-12,14,20-29,34-35, and 39-48 are examined on the merits.

New Arguments

Claim Rejections - 35 USC § 112, 1st paragraph

5. Claims 1,3-12,14,20-29,34-35, and 39-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION. The claims recite the limitation of "other than said at least first antibody, or an antigen binding fragment thereof" as part of the invention. However, the specification or claims as originally filed failed to support the negative limitation of "other

than said at least first antibody, or an antigen binding fragment thereof". In the amendment filed 6/20/2002, applicant points to page 104, lines 22-24 of the specification for support of the negative proviso. However, the limitation of "other than" is not supported by that specific disclosure, because the specification only indicates that anti-aminophospholipid antibodies and "other anti-cancer agents" can be separated from one another when in kit form. The specification does not support a second anti-cancer agent other than the first anti-cancer agent. In fact, the specification specifically teaches that the first and second anti-cancer agent can be the same (see page 32, for example). Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Claim Rejections - 35 USC § 112, 1st paragraph

6. Claims 1,3-12,14,20-21,34,39,40-45, and 47-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth a kit or therapeutic kit comprising at least a first anti-cancer agent, wherein the first anti-cancer agent is an antibody that binds to aminophospholipids, and at least a second anti-cancer agent that is a chemotherapeutic, radiotherapeutic, anti-angiogenic, or apoptotis inducing agent and therefore the written description in this case is not commensurate in scope to the

claims that read on a kit comprising a first anti-cancer agent, wherein the anti-cancer agent is an antibody, and at least the second anti-cancer is any and all anti-cancer agents.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115). The following *written description* rejection is set forth herein.

The claims recite a "at least a second anti-cancer agent other than said first at least a first antibody or ant antigen binding fragment thereof" as part of the invention. However, there does not appear to be an adequate written description in the specification as-filed of the essential structural feature or a representative number of species that are representative of the broad genus of "second anti-cancer" agents encompassed by the claims. The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e.,

structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Applicant does not appear to have reduced to practice a representative number of second anti-cancer agents. Neither has Applicant provided a sufficient written description of any structure that may be correlated with the desired antagonistic function of preventing cancer. An "anti-cancer agent" encompasses *any* molecule with the functional activity of inhibiting or treating cancer. This class of compounds includes proteins, nucleic acids, small molecules, inorganic, or organic compounds, all of which has not been adequately represented in the specification as filed. Thus the genus of compounds encompassed by this term is extensive and the artisan would not be able to recognize that Applicant was in possession of the invention as now claimed.

Consequently, Applicant was not in possession of the instant claimed invention. See Regents of the University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention." Id. 43 USPQ2d at 1404 (quoting Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406. A description of what the genetic

material does, rather than of what it is, does not suffice. Id. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is invited to point to clear support or specific examples of the claimed invention in the specification as-filed.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-11, 14, 20-24,27-29, and 39-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 59-64

of U.S. Patent No. 6,818,213. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant invention encompasses is a genus claims that encompasses the narrower species taught in the issued US Patent 6,818,213. In particular, the claims of the issued US Patent are drawn to a composition comprising a first binding ligand that has comprises a targeting agent that localizes to aminophospholipids, wherein the targeting agent is an anti-phosphotidylserine antibody, and further comprising a second anti-cancer agent.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit comprising an at least a first anti-cacner agnet, wherein the agent is an antibody against aminophospholipid and further comprising a second anti-cancer agent which is other than the first anti-cancer agent as claimed, because the issued US patent provides sufficient motiviation and expectation of success in doing so. One of skill would have been motivated in doing so primarily because an species (i.e. the issued US patent) obviates a genus (i.e. instant invention).

Claim Rejections Maintained - 35 USC § 103

9. The rejection of claims 1,3-12,14,19-29,34,35,39-43 under 35 USC § 103(a) as being obvious over Schroit *et al* in view of Gimbrone, Umeda *et al*, and Byers is maintained for the reasons of record. Applicant argues that the combination of the references do not support a *prima facie* case of obviousness. In particular applicant argues that the addition of Byers does not provide sufficient motivation because the field of antibody immunology is vast. Applicant additionally contends that the cited

references teach subject matter used for difference purposes and have different content which cannot be combined together to teach the instantly claimed kit. Applicant also contends that instant invention provides a surprising discovery and overcomes problems associated with immunotoxins. Specifically applicant indicates that the important difference in the instant invention is the use of naked or unconjugated antibodies. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the prior art teaches antibodies directed against phosphotidylserine (PS) and the prior art teaches numerous second anti-cancer agents, such as those taught by Gimbrone.. Thus the combination of the references to make a product useful for the purposes of treating cancers associated with tumor vasculature would be obvious.

Objective evidence or secondary considerations such as unexpected results, commercial success, long-felt need, failure of others, copying by others, licensing, and skepticism of experts are relevant to the issue of obviousness and must be considered in every case in which they are present. When evidence of any of these secondary considerations is submitted, the examiner must evaluate the evidence. The weight to be accorded to the evidence depends on the individual factual circumstances of each case.

Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In the instant case, applicant indicates that the use of "naked" or unconjugated antibodies is unexpected, however the applicant has not supplied any objective evidence that the use of such antibodies is in fact "surprising". Instead applicant only asserts that such is true. The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). In addition, not all claims are drawn to "naked" or unconjugated antibodies as argued. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Therefore the rejection of the claims under 35 USC 103(a) as being obvious is maintained for the reasons of record.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 12/9/2004.

Conclusion

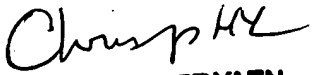
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1643
August 18, 2005



CHRISTOPHER YAEN
PATENT EXAMINER